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(54) Title: NUTRITIONAL COMPOSITION FOR AN IMMUNE CONDITION

(57) Abstract: A nutritional composition is described for prevention or treatment of an immune condition. It comprises, in a broad definition, at least vitamin E, vitamin C, vitamin B6, folic acid, vitamin B12, copper, zinc, selenium, fructo-oligosaccharides and/or inulin, a probiotic lactic acid bacterium. For example, in an embodiment it comprises per 300g: 150IU Vitamin E, 120 mg Vitamin C, 2mg Vitamin B6, 400ug Folic acid, 3.8ug Vitamin B12, 1.5mg Copper, 15mg Zinc, 100ug Selenium, 3g Fructo-oligosaccharides and/or inulin, 10E10 cfu ST11 lactobacillus. A method for making it; use of it in the manufacture of a functional food or medicament; and a method of prevention or treatment of an immune condition which comprises administering an effective amount of the composition are described.

Nutritional Composition For an Immune Condition

The present invention relates to a nutritional composition for prevention or treatment of an immune condition, a method of production of the composition, use of the composition in the manufacture of a functional food or medicament for the prevention or treatment of an immune condition and a method of treatment of an immune condition which comprises administering an effective amount of the composition.

Within the context of this specification the word "comprises" is taken to mean "includes, among other things". It is not intended to be construed as "consists of only".

Within the context of this specification the term "an immune condition" represents an ailment selected from the group which comprises an impaired immune response, an inflammatory condition, inflammation, chronic disease (for example arthritis or gastritis), conditions associated with aging and leading to an increase of inflammatory responses.

Americans greater than 65 years old, at the turn of the century, accounted for 4% of the US population; currently, they account for greater than 12% of the population. However, although they only account for 12% of the US population, they account for greater than 40% of acute hospital bed days, buy greater than 30% of all prescription drugs and spend 30% of the US health budget. Furthermore, it has been estimated that in 2030, greater than 70 million Americans (1:5) will be over the age of 65, and those over 85 are expected to experience the highest percentage increase of all age groups.

As the average age of the population increases, obtaining a better understanding of the unique aspects of aging in relation to nutritional needs and treatment is imperative. Many physiologic functions decline progressively throughout adult life and have an impact on nutrition. For instance, a reduction in the number of functioning cells and the resultant slowing of metabolic processes results in a

decrease in caloric requirements among the elderly. Also, the reduction in physical activity that generally accompanies aging further decreases energy requirements. Merely decreasing the total caloric intake of an elderly patient may adversely affect their required nutrition. When the total caloric intake is reduced, the remaining food intake must carefully insure a properly balanced intake of proteins, vitamins and minerals. To reduce caloric intake in the elderly, consumption of "empty" calories (i.e. fats) can be reduced and consumption of nutrient-dense foods (i.e. carbohydrates and proteins) can be increased.

While the nutritional needs of the mature adult differ from those of an adult, in health care settings, standard nutritional formulae are the primary form of elemental nutrition currently used. Naturally, standard formulae do not take into account the nutritional needs of an elderly patient. Standard products suffer from the problem that they must be supplemented with key micronutrients to compensate for common deficiencies and metabolic changes of an elderly patient. Therefore, a need exists for a nutritional composition which meets the nutritional needs of an elderly patient.

In addition to the above problems, a composition is required to address the problems of immune conditions in the elderly as well as in clinical and performance settings, for example, with regard to an athlete recovering from injury.

Furthermore, it is known that the effects of diet and nutritional supplements can play a role in improving the survival and quality of life. In particular, a need exists for a nutritional composition which can help to improve health, in particular with regard to an immune condition.

Furthermore, it is known that the problem of an impaired immune response can be associated with aging, chronic pathological conditions and/or malnutrition. This problem has been partly addressed by providing nutritional supplements. However, these supplements suffer from the problem that, generally, they are specific for certain ailments and do not provide good nutritional support for patients suffering from a more complicated combination of conditions. This is particularly relevant with respect to an elderly patient. In addition, the increase in the likelihood of

chronic disease such as arthritis, gastritis, etc, with age leads to an increase in inflammatory reactions.

Furthermore, a need exists for a nutritional composition which addresses the problems associated with infectious diarrhoea (rotavirus and bacterial infection), allergy, restoration of and maintenance of gut integrity, bacterial overgrowth, endotoxemia and gut permeability.

The present invention addresses the problems set out above.

Remarkably, a composition has now been found that can be used to provide nutrition to an elderly patient, as well as performance nutrition eg to an athlete, or clinical nutrition to a hospital patient.

Accordingly, in a first aspect, the present invention provides a composition which comprises a source of protein, a source of carbohydrate, a source of fat, a probiotic lactic acid bacterium and additionally fructo-oligosaccharides and/or inulin.

In a second aspect the invention provides a method of producing a composition according to an embodiment of the invention which comprises the step of blending the required nutrients together in the required amounts.

In a third aspect the invention provides use of a composition according to the invention in the prevention or treatment of an immune condition.

In a fourth aspect the invention provides use of a composition according to an embodiment of the invention in the manufacture of a functional food or a medicament for the prevention or treatment of an immune condition.

In a fifth aspect the invention provides a method of prevention or treatment of an immune condition which comprises administering an effective amount of a composition according to an embodiment of the invention.

Preferably, an embodiment of a composition according to the invention comprises one or more nutrients or minerals selected from the group consisting of vitamin E, vitamin C, vitamin B6, folic acid, vitamin B12, copper, zinc and selenium. More preferably, it comprises at least two of these nutrients or minerals. Even more preferably, it comprises at least three of these nutrients or minerals. Most preferably it includes all of these minerals or nutrients.

Preferably, an embodiment of a composition according to the invention additionally comprises one or more nutrients or minerals selected from the group consisting of calcium, phosphorus, magnesium, iron, vitamin A, vitamin B1, vitamin B2, niacin and vitamin D. More preferably, it comprises at least two of these nutrients or minerals. Even more preferably, it comprises at least three of these nutrients or minerals. Most preferably an embodiment of a composition according to the invention includes all of these minerals or nutrients.

Preferably, an embodiment of a composition according to the invention comprises calcium in the form of milk calcium or calcium derived from milk calcium.

Preferably, an embodiment of a composition according to the invention comprises one or more probiotic lactic acid bacteria selected from the group which consists of paracasei and johnsonii bacteria. More preferably, an embodiment of a composition according to the invention comprises one or more probiotic lactic acid bacteria selected from the group which consists of ST11 (deposited under the number NCCMI-2116) and La1 (deposited under the number NCCMI-1225).

Preferably, an embodiment of a composition according to the invention comprises the following masses or amounts of nutrients or minerals (if present) per 300g of the composition. Preferably, this is the amount of composition administered per day.

Vitamin E: preferably about 1 IU to about 400 IU, most preferably about 120 IU
Vitamin C: preferably about 6 mg to about 300 mg, most preferably about 120 mg
Vitamin B6: preferably about 0.17 mg to about 3 mg, most preferably about 2 mg
Folic acid: preferably about 40 ug to about 800 ug, most preferably about 400 ug

Vitamin B12: preferably about 0.24 mg to about 5mg, most preferably about 3.8 ug
Copper: preferably about 0.3 mg to about 3 mg, most preferably about 1.5 mg
Zinc: preferably about 1.5 mg to about 15 mg, most preferably about 15 mg
Selenium: preferably about 7 ug to about 300 ug, most preferably about 100 ug
Fructo-oligosaccharides and/or gum acacia: preferably about 4 g to about 50 g, most preferably about 6g
Lactic acid bacteria: preferably about 10E8 to about 10E12 cfu, most preferably about 10E10 cfu.

Preferably, an embodiment of a composition according to the invention comprises one or more nutrients selected from the following masses or amounts of nutrients or minerals (if present) per 300g of the composition. Preferably, this is the amount of composition administered per day.

calcium: about 100mg to about 300 mg, more preferably about 200mg;
phosphorus: about 50mg to about 615mg, more preferably about 150mg ;
magnesium: about 110mg to about 210mg, more preferably about 60mg;
vitamin A: about 1000IU to about 1500IU, more preferably about 1333IU;
vitamin D: about 50IU to about 150IU, more preferably about 100IU;
vitamin E: about 5.0 IU to about 150 IU, more preferably about 120IU;
vitamin C: about 30mg to about 500mg, more preferably about 120mg;
vitamin B1: about 0.1mg to about 2mg, more preferably about 0.25mg;
vitamin B2: about 0.1mg to about 0.6mg, more preferably about 0.3mg;
niacin: about 1.5mg to about 7.2mg, more preferably about 3mg;
vitamin B6: about 1.0mg to about 3.0mg, more preferably about 2mg;
folic acid: about 200ug to about 600ug, more preferably about 400ug;
vitamin B12: about 1.5ug to about 4.5ug, more preferably about 3.8ug;
iron: about 2.0mg to about 5mg, more preferably about 2.75mg; and
zinc: about 10mg to about 20mg, more preferably about 15mg.

Preferably, an embodiment of a composition according to the invention comprises gum acacia.

Preferably, an embodiment of a method according to the invention comprises the steps of blending the nutrients in the required amounts and extruding the blended mixture. More preferably it includes spray drying the mixture.

An advantage of the present invention is that it provides a nutritional composition that can be dissolved instantaneously in water to provide a beverage or soup. It does not require cooking.

Another advantage of the present invention is that it provides a single composition that can be adapted and administered simply in a food for the prevention or treatment an immune condition. The composition can be provided in clinical or performance nutrition settings and is particularly suitable for an elderly patient.

Advantages provided by the probiotic bacteria include prevention or inhibition of diarrhea brought about by pathogenic bacteria; prevention or inhibition of diarrhea, especially infections of intestinal cells by rotavirus; prevention of colonization of the intestine by pathogenic bacteria causing diarrhea; and an ability to adhere to and colonise the intestinal mucosa of a host organism.

Yet another advantage of the present invention is that it provides a composition beneficial for diabetics. This is due to the specific composition of macronutrients, protein, carbohydrate and fat which provides a low glycemic index.

Additional features and advantages of the present invention are described in, and will be apparent from the description of the presently preferred embodiments which are set out below.

For the purposes of clarity and a concise description features are described herein as part of the same or separate embodiments, however it will be appreciated that the scope of the invention may include embodiments having combinations of all or some of the features described.

In an embodiment, a nutritional composition comprises a source of protein. The protein source preferably provides about 5% to about 55% of the energy of the nutritional formula; for example about 20% to about 50%, preferably 26%, of the energy. Dietary protein is preferred as a source of protein. The dietary protein may be any suitable dietary protein; for example animal protein (such as milk protein,

meat protein or egg protein); vegetable protein (such as soy protein, wheat protein, rice protein, and pea protein); a mixture of free amino acids; or a combination thereof. Milk proteins such as casein, whey proteins and soy proteins are particularly preferred.

The composition also comprises a source of carbohydrates and a source of fat.

A fat source preferably provides about 5% to about 55% of the energy of the nutritional formula; for example about 20% to about 50%, preferably 23%, of the energy. Lipid making up the fat source may be any suitable fat or fat mixture. Vegetable fat is particularly suitable; for example soy oil, palm oil, coconut oil, safflower oil, sunflower oil, corn oil, canola oil, lecithins, and the like. Most preferably it is a mixture of canola and soy oils. Animal fat such as milk fat may also be added if desired.

Preferably the composition comprises saturated fat which preferably comprises about 1% to about 5%, more preferably 2.5% of the total energy of the product. Preferably it comprises monounsaturated fat which preferably comprises about 5% to about 15%, more preferably 9.9% of the total energy of the product. Preferably the composition comprises polyunsaturated fat which preferably comprises about 5% to about 15%, more preferably 10.1% of the total energy of the product. Preferably the composition comprises linoleic acid which preferably comprises about 5% to about 15%, more preferably 8.5% of the total energy of the product. Preferably the composition comprises linolenic acid which preferably comprises about 0.5% to about 5%, more preferably 1.6% of the total energy of the product. Preferably the ratio of linoleic acid to linolenic acid is about 3 to about 8, more preferably about 5.3.

A source of carbohydrate preferably provides about 40% to about 80%, more preferably about 51% of the energy of the nutritional composition. Any suitable carbohydrate may be used, for example sucrose, lactose, glucose, fructose, corn syrup solids, maltodextrin, or a mixture thereof.

This embodiment of the composition additionally comprises about 10E10 cfu of paracaseii or johnsonii probiotic lactic acid bacteria and about 6g of fructooligosaccharide and inulin per 300g of the composition.

Dietary fibre may also be added. Preferably dietary fibre provides up to about 5% of the energy of the nutritional composition. The dietary fibre may be from any suitable origin, preferably fructooligosaccharide, inulin, or a mixture thereof.

Additional suitable vitamins and minerals are included in the composition as described above.

Monosodium glutamate may be added as a flavour enhancer.

The nutritional composition is preferably enterally administrable; for example in the form of a powder, a liquid concentrate, or a ready-to-drink beverage. If it is desired to produce a powdered nutritional formula, the homogenized mixture is transferred to a suitable drying apparatus such as a spray drier or freeze drier and converted to powder.

Alternatively, a usual food product may be enriched with an embodiment of composition. For example, a fermented milk, a yogurt, a fresh cheese, a renneted milk, an article of confectionery, for example a sweet or sweetened beverage, a confectionery bar, breakfast cereal flakes or bars, a drink, milk powder, soy-based product, non-milk fermented product or a nutritional supplement for clinical nutrition. Then, the amount of the composition added is preferably at least about 0.01% by weight.

The following examples are given by way of illustration only and in no way should be construed as limiting the subject matter of the present application. Percentages and parts are by weight unless otherwise indicated.

Examples 1 and 2: Nutritional Compositions

Two nutritional compositions were made by blending the required constituents. Their compositions are indicated below in table 1. The compositions are intended to be consumed in the form of two oral supplements per day based on enriched beverages or milk product desserts. The total daily dose is intended to be approximately 300g or 300ml of composition.

Table 1

	Daily dose 300ml/day	Daily dose 300ml/day
Energy P/L/C %TEI	480kcal (1.6kcal/ml) 26% / 24% / 51%	300kcal (1.0kcal/ml) 28% / 30% /42%
Protein g/100 ml	10.5 (with 6.25 g soy protein)	7.0
Fat g/100ml	4.16	3.3
Carbohydrate g/100ml	20.6	10.5
in daily dose	per 300ml	per 300ml
Na mg	188	188
K mg	350	350
Cl mg	290	290
Ca mg	200	200
P mg	150	150
Ca/P ratio	1.3	1.3
Mg mg	60	60
Mn ug	495	495
A IU	1333	1333
D IU	100	100
E IU	120	150
K1 ug	13.8	13.8
C mg	120	120
B1 mg	0.25	0.25
B2 mg	0.3	0.3
Niacin mg	3	3
B6 mg	2.0	2.0
Folic acid ug	400	600
Panto mg	1.00	1.00
B12 ug	3.8	10.0
Biotin ug	7.5	7.5
Fe mg	2.75	2.75
I ug	75	75
Cu mg	1.5	1.5
Zn mg	15	6
Se ug	100	100
Cr ug	12.5	12.5
Mo ug	18.75	18.75
Inulin & FOS blend (30:70 blend) g	6	6
Lactobacillus cfu/serving	Paracaseii 10^{10}	Johnsonii 10^{10}

It should be understood that various changes and modifications to the presently preferred embodiments described herein will be apparent to those skilled in the art. Such changes and modifications can be made without departing from the spirit and

scope of the present invention and without diminishing its attendant advantages. It is therefore intended that such changes and modifications be covered by the appended claims.

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Claims

1. A composition which comprises a source of protein, a source of carbohydrate, a source of fat, a probiotic lactic acid bacterium and additionally fructo-oligosaccharides and/or inulin.

2. A composition according to claim 1 which comprises one or more nutrients or minerals selected from the group consisting of vitamin E, vitamin C, vitamin B6, folic acid, vitamin B12, copper, zinc and selenium.

3. A composition according to claim 2 wherein the composition comprises at least three nutrients or minerals selected from the group consisting of vitamin E, vitamin C, vitamin B6, folic acid, vitamin B12, copper, zinc and selenium.

4. A composition according to claim 2 or 3 wherein the composition comprises vitamin E, vitamin C, vitamin B6, folic acid, vitamin B12, copper, zinc and selenium

5. A composition according to any preceding claim which comprises one or more nutrients or minerals selected from the group consisting of calcium, phosphorus, magnesium, iron, vitamin A, vitamin B1, vitamin B2, niacin and vitamin D.

6. A composition according to claim 5 wherein the composition comprises at least three nutrients or minerals selected from the group consisting of calcium, phosphorus, magnesium, iron, vitamin A, vitamin B1, vitamin B2, niacin and vitamin D.

7. A composition according to claim 5 or 6 wherein the composition comprises calcium, phosphorus, magnesium, iron, vitamin A, vitamin B1, vitamin B2, niacin and vitamin D.

8. A composition according to any one of claims 5 to 7 wherein calcium is in the form of milk calcium or calcium derived from milk calcium.

9. A composition according to any preceding claim which comprises one or more probiotic lactic acid bacterium selected from the group which consists of paracasei and johnsonii bacteria.

10. A composition according to claim 9 wherein the lactic acid bacterium is selected from the group consisting of ST11 (deposited under the number NCCMI-2116) and La1 (deposited under the number NCCMI-1225).

11. A composition according to any preceding claim wherein the composition comprises the following masses or amounts of nutrients or minerals (if present) per 300g of the composition:

Vitamin E: about 1 IU to about 400 IU,
Vitamin C: about 6 mg to about 300 mg,
Vitamin B6: about 0.17 mg to about 3 mg,
Folic acid: about 40 ug to about 800 ug,
Vitamin B12: about 0.24 mg to about 5mg,
Copper: about 0.3 mg to about 3 mg,
Zinc: about 1.5 mg to about 15 mg,
Selenium: about 7 ug to about 300 ug,
Fructo-oligosaccharides and/or inulin: about 4 g to about 50 g,
Lactic acid bacteria: about 10E8 to about 10E12 cfu.

12. A composition according to any preceding claim wherein the composition comprises the following masses or amounts of nutrients or minerals (if present) per 300g of the composition:

calcium: about 100mg to about 300 mg,
phosphorus: about 50mg to about 615mg,
magnesium: about 110mg to about 210mg,
vitamin A: about 1000IU to about 1500IU,
vitamin D: about 50IU to about 150IU,
vitamin E: about 5.0 IU to about 150 IU,

vitamin C: about 30mg to about 500mg,
vitamin B1: about 0.1mg to about 2mg,
vitamin B2: about 0.1mg to about 0.6mg,
niacin: about 1.5mg to about 7.2mg,
vitamin B6: about 1.0mg to about 3.0mg,
folic acid: about 200ug to about 600ug,
vitamin B12: about 1.5ug to about 4.5ug,
iron: about 2.0mg to about 5mg,
zinc: about 10mg to about 20mg.

13. A composition according to any preceding claim which comprises gum acacia.

14. A method of producing a composition according to any preceding claim which comprises the step of blending the required nutrients together in the required amounts.

15. A method according to claim 13 which comprises the additional steps of extruding the blended mixture and/or spray drying the mixture.

16. Use of a composition according to any one of claims 1 to 13 in the prevention or treatment of an immune condition.

17. Use of a composition according to any one of claims 1 to 13 in the manufacture of a functional food or a medicament for the prevention or treatment of an immune condition.

18. A method of prevention or treatment of an immune condition which comprises administering an effective amount of a composition according to any one of claims 1 to 13.

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A23L1/29 A23L1/302 A23L1/304 A61K35/74 A23L1/03
A23C9/123 A23L1/0528

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A23L A61K A23C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BIOSIS, MEDLINE, FSTA, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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Y	--- -/--	9,10

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

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Date of the actual completion of the international search	Date of mailing of the international search report
30 April 2002	07/05/2002

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Couzy, F

INTERNATIONAL SEARCH REPORT

Int tional Application No
PCT/EP 01/13302

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
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